Population pharmacokinetics of cefazolin in morbidly obese patients upon a prophylactic dose of 2 gram for weight reducing surgery

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OBJECTIVES

Morbid obesity is an independent risk factor for the development of surgical site infections. Before weight reducing surgery an i.v. dose of cefazolin 2 gram is given for prophylaxis of surgical site infections. In this study we aimed to investigate the population pharmacokinetics of cefazolin in morbidly obese patients undergoing weight reducing surgery.

METHODS

At induction of anesthesia morbidly obese patients received an i.v. dose of cefazolin 2 gram. Blood samples were drawn at T=0, 5, 10, 30, 60, 120, 180 and 240 min after dosing and were analyzed using HPLC-UV. Cefazolin plasma concentrations were modelled using NONMEM VI and S-PLUS. A step-wise covariate analysis was performed to identify the influence of total body weight, lean body weight, ideal body weight, body mass index (BMI), age, sex, creatinine and bilirubin on the pharmacokinetics of cefazolin.

RESULTS

Twenty morbidly obese patients with a median total body weight of 144 kg (range 112-252 kg), a median BMI of 51 kg/m² (range 38-79), a median age of 48 years (range 22-59) and a median creatinine of 63 µmol/L (range 31-144) were included in the study. In a two compartment model (ADVAN 3 TRANS) total body weight proved the most predictive covariate for central volume of distribution (linearly centred) with inter-individual variability decreasing from 21.7% to 12.4% (p < 0.001) compared to simple model.

CONCLUSION

We developed a two compartment pharmacokinetic model for cefazolin in morbidly obese patients in which total body weight and age or creatinine proved to be the major determinants for respectively central volume of distribution and clearance. Plasma concentrations profiles in lean patients are awaited to confirm the currently observed covariate relations for the pharmacokinetic parameters of cefazolin.